that claims 2-6, 9, 11, 12, 15, 20, and 21 are allowable if rewritten in independent form. The Examiner has indicated that claims 54 and 55 are allowed. In this response, claims 1 and 31 are amended, and new claims 56-65 are presented for examination on their merits.

Applicants bring to the Examiner's attention a clerical error in the section entitled "Election/Restrictions". The Examiner states that claims 31-32 are withdrawn. However, these claims are part of the elected group and appear to have been substantively examined. Accordingly, Applicants request clarification of the status of claims 31-32.

Claims 1, 8, 10, 13, 14, 16-19, 31, 40, 42, 45, 46, 48, 49, 50, and 51 are rejected under 35 U.S.C. § 102(b) as being allegedly anticipated by Wang *et al.*, *Glycobiology*, Vol. 6(8):837-842 (1996). Claims 7 and 39 are rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Wang *et al.* as applied to claims 1, 8, 10, 13, 14, 16-19, 31, 40, 42, 45, 46, 48, 49, 50, and 51, and further in view of Ge Wang *et al.*, *Microbiology*, Vol. 145:3245-3253 (1999). Claims 31-53 are rejected under 35 U.S.C. § 112, second paragraph for allegedly being vague and indefinite. Applicants respond to the objections and rejections with a combination of amendment and traversal.

The Invention

The examined claims are drawn to methods for modifying glycosylation patterns of glycopeptides, including recombinantly produced glycopeptides. Also provided are glycopeptide compositions in which the glycopeptides have a uniform glycosylation pattern.

The Amendments

Claims 1 and 31 are amended to recite that the fucosyltransferase lacks a membrane anchoring domain. Support for these amendments is found at page 12, lines 10-15 of the specification.

New claim 56 is claim 2 rewritten in independent form. New claim 57 is claim 3 rewritten in independent form. New claim 58 is claim 4 rewritten in independent form. New claim 59 is claim 5 rewritten in independent form. New claim 60 is claim 6 rewritten in independent form. New claim 61 is claim 8 rewritten in independent form. New claim 62 is claim 9 rewritten as dependent upon claim 61. New claim 63 is claim 15 rewritten in independent form. New claim 64 is claim 20 rewritten in independent form. New claim 65 is

claim 21 rewritten in independent form. The Examiner states that the subject matter of each of claims 2-6, 8-9, 15, 20 and 21 are allowable if rewritten in independent form. Accordingly, Applicants request a notification of the allowability of new claims 56-65.

Applicants have presented claims that are similar in scope to the claims that were examined. Neither the new claims nor the amended claims are outside of the Group originally elected, nor are they inconsistent with the election of species.

No new matter has been added by either the new or amended claims.

The Rejections

Under 35 U.S.C. § 112, Second Paragraph

Claims 31-53 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Examiner alleges that "substantially identical" in claims 31 and 32 is indefinite without recitation of how much fucosylation is "substantial". Applicants respectfully traverse this rejection.

The test for definiteness is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity in light of, among other things, the application disclosure. MPEP § 2173.02. Applicants submit that the definition of "substantially" as defined on page 15, lines 16-20 satisfies this test.

At page 15, lines 16-20 of the specification as filed it is stated that,

> The term "substantially identical fucosylation pattern," refers to a glycosylation pattern of a glycopeptide produced by a method of the invention which is at least about 80%, more preferably at least about 90%, even more preferably at least about 95% and still more preferably at least about 98% identical to the fucosylation of a known glycoprotein.

Thus, the specification includes a numerical value for the term "substantially" in "substantially identical". One of skill in the art would recognize that the phrase "fucosylation pattern that is

substantially identical to a fucosylated glycopeptide", from claim 31, is encompassed by the term "substantially identical fucosylation pattern" mentioned above.

In view of the evidence set forth above, Applicants have established the adequacy of definiteness sufficient to support claims 31-53. Therefore, Applicants respectfully request the withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Under 35 U.S.C. § 102(b)

***Over Wang et al.* ("Wang")**

Claims 1, 8, 10, 13, 14, 16-19, 31, 40, 42, 45, 46, 48, 49, 50, and 51 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Wang *et al.*, *Glycobiology*, Vol. 6(8):837-842 (1996). To maintain a *prima facie* case of anticipation, the Examiner must demonstrate that each and every element as set forth in the claim is found, either expressly or is inherently described in a single prior art reference. The identical invention must be shown in as complete detail as is contained in the ...claim. See MPEP § 2131. Applicants submit that each element of the claims now pending has not been identified in the art presently of record.

Wang teaches a method of fucosylating a peptide using a fucosyltransferase. On lines 38-40 of column 2 of page 840, Wang states that "the enzyme [fucosyltransferase] is probably a membrane protein". One of skill in the art would understand that a membrane protein includes a membrane anchoring domain. Applicants have amended claims 1 and 31 to recite a fucosyltransferase which lacks a membrane anchoring domain.

Because Wang does not teach the element of a fucosyltransferase which lacks a membrane anchoring domain, Wang does not disclose each and every element of claims 1, 8, 10, 13, 14, 16-19, 31, 40, 42, 45, 46, 48, 49, 50, and 51. Accordingly claims 1, 8, 10, 13, 14, 16-19, 31, 40, 42, 45, 46, 48, 49, 50, and 51 are in condition for allowance and Applicants respectfully request withdrawal of the rejection.

In addition to the novelty of claims 1 and 31, Wang does not disclose every element of claims 8, 13, 14, 16-18, 40, 45, 48, 49, and 50.

Wang does not disclose every element of either claims 8 or 40

On page 4, line 5 of the Office Action, the Examiner states that Wang discloses fucosyltransferases that are recombinantly produced. However, in the "Materials and Methods"

section in column 2 on page 841, Wang states that the O-fucosyltransferase is partially purified from Chinese hamster ovary (CHO) cell paste (line 5) and also purified from rat liver (line 23). Applicants have reviewed the Materials and Methods section, and it is silent concerning recombinant production of fucosyltransferases. The purified fucosyltransferase from CHO cell paste in Wang is from a natural source. Therefore, Wang teaches the purification of O-fucosyltransferase, ***not its recombinant production***.

Because Wang does not teach the element of recombinant production of fucosyltransferases found in Applicants' invention, Wang does not demonstrate each and every element of claims 8 and 40. Therefore, Applicants respectfully request the withdrawal of the rejection under 35 U.S.C. § 102(b).

Wang does not disclose every element of either claims 13 or 45

On page 4, line 6 of the Office Action, the Examiner states that Wang discloses the use of full-length glycopeptides. However, in the "Materials and Methods" section in lines 33-38 in column 1 on page 841, Wang states,

> A recombinant form of the first EGF domain from human factor VII was produced in *E.coli*. ***This construct included residues 45-87*** of the intact protein, an amino-terminal hexahistidine tag and three additional residues not of factor VII origin at the carboxy terminus, for the following primary sequence:
> HHHHHHSDGDQCASSPCQNGGSC
> KDQLQSYICFCLPAFEGRNCETHKDDGSA. [emphasis added]

Because of the use of a sugar-lacking domain (i.e. residues 45-87) from the larger human factor VII protein, Wang teaches the use of peptide ***fragments***, not full-length ***glyco***peptides.

Because Wang does not teach the element of using full-length glycopeptides found in the Applicants' invention, Wang does not demonstrate each and every element of claims 13 and 45. Therefore, Applicants respectfully request the withdrawal of the rejection under 35 U.S.C. § 102(b).

Wang does not disclose every element of either claims 16 or 48

Claims 16 and 48 have been amended to change their dependency from claims 1 and 31, respectively, to claims 13 and 45, respectively. As discussed above, elements are lacking from claims 13 and 45. Those elements are also lacking from subsequent dependent claims such as 16 and 48. Therefore, Applicants respectfully request the withdrawal of the rejection under 35 U.S.C. § 102(b).

Wang does not disclose every element of either claims 17 or 49

On page 4, line 7 of the Office Action, the Examiner states that Wang teaches glycopeptides located on cells. In fact, after the purification procedures in Wang, the glycopeptide fragments cannot be located on cells. On lines 34-47 of column 1 on page 841, Wang subjects a cell ***lysate*** to a Sepharose column containing $NiSO_4$. The glycopeptide fragment containing an amino-terminal hexahistidine tag remains attached to the nickel in the Sepharose column, while the rest of the cell lysate is eluted. Wang separately elutes the purified glycopeptide fragment by adding imidazole to the column (lines 50-51). Therefore, Wang teaches a glycopeptide fragment that is free in solution, ***not glycopeptides located on cells***.

Because Wang does not teach the element of glycopeptides localized on cells, Wang does not demonstrate each and every element of claims 17 and 49. Therefore, Applicants respectfully request the withdrawal of the rejection under 35 U.S.C. § 102(b).

Wang does not disclose every element of either claims 18 or 50

In the Office Action, the Examiner rejected claims 18 and 50 under 35 U.S.C. § 102(b). Applicants claim "acceptor moieties comprising Galβ1-OR, Galβ1,3/4GlcNAc-OR, NeuAcα2,3Galβ1,3/4GlcNAc-OR, wherein R is an amino acid, a saccharide, an oligosaccharide or an aglycon group having at least one carbon atom and is linked to or is part of a glycopeptide". Applicants have reviewed Wang, and are unable to find references to the fucosylation of a glycopeptide ***through a galactose moiety***. In fact, Wang discloses the addition of "fucose through an O-glycosidic linkage to a conserved ***serine*** or ***threonine*** residue in EGF domains," (lines 3-5, Abstract, p. 837). Therefore, Wang discloses an ***amino acid acceptor moiety***, rather than a sugar acceptor moiety, such as that claimed by Applicants.

Because Wang does not teach the element of fucosylating a glycopeptide through a sugar moiety, Wang does not disclose each and every element of claims 18 and 50. Therefore, Applicants respectfully request that the withdrawal of the rejection under 35 U.S.C. § 102(b).

Under 35 U.S.C. § 103(a)

Over Wang and further in view of Ge Wang et. al. ("Ge")

Claims 7 and 39 are rejected as being allegedly obvious under 35 U.S.C. § 103 (a) over Wang in view of Ge.

To construct a *prima facie* case of obviousness, the Examiner must meet three criteria. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references) must teach or suggest all of the claim limitations. *See*, MPEP § 2142. Moreover, to avoid the pitfall of hindsight, the Examiner must "identify specifically...the reasons one of ordinary skill in the art would have been motivated to select the references and combine them," *In re Rouffet* 47 USPQ2d 1453, 1459 (Fed. Cir. 1998). Applicants respectfully submit that the third criteria has not been met.

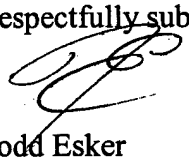
Wang teaches a method of fucosylating a peptide where the fucosyltransferase possesses a membrane anchoring domain. On page 5, lines 19-20 of the Office Action, the Examiner states that Ge teaches a fucosyltransferase from a bacteria, *Helicobacter pylori*. Applicants have amended claims 1 and 31 to recite a fucosyltransferase which lacks a membrane anchoring domain. Because claim 39 is dependent upon claim 31, it also contains this limitation. Because Wang and Ge do not disclose the element of a fucosyltransferase which lacks a membrane anchoring domain, Applicants assert that the *prima facie* case for obviousness has not been made. Therefore, Applicants respectfully request the withdrawal of the rejection under 35 U.S.C. § 103(a).

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. (Amended) A method for modifying the glycosylation pattern of a glycopeptide comprising an acceptor moiety for a first fucosyltransferase wherein said first fucosyltransferase lacks a membrane anchoring domain, said method comprising:

contacting the glycopeptide with a reaction mixture that comprises a fucose donor moiety and the first fucosyltransferase under appropriate conditions to transfer fucose from the fucose donor moiety to the acceptor moiety, such that the glycopeptide has a substantially uniform fucosylation pattern.

31. (Amended) A method of producing a recombinant glycopeptide having a fucosylation pattern that is substantially identical to a fucosylated glycopeptide having a known fucosylation pattern, said method comprising:

(a) contacting the recombinant glycopeptide with a reaction mixture that comprises a fucose donor moiety and the fucosyltransferase under appropriate conditions to transfer fucose from the fucose donor moiety to a fucose acceptor moiety on said recombinant glycopeptide, thereby producing a fucosylated recombinant glycopeptide, wherein said fucosyltransferase lacks a membrane anchoring domain; and

(b) terminating the transfer of the fucose to the fucose acceptor when the fucosylation pattern substantially identical to the known fucosylation pattern is obtained.

56. (New) A method for modifying the glycosylation pattern of a glycopeptide comprising a first acceptor moiety for a first fucosyltransferase and a second acceptor moiety for a second fucosyltransferase, said method comprising:

(a) contacting the glycopeptide with a reaction mixture that comprises a fucose donor moiety and the first fucosyltransferase under appropriate conditions to transfer fucose from the fucose donor moiety to the first acceptor moiety, such that the glycopeptide has a substantially uniform fucosylation pattern, and

(b) contacting the glycopeptide with a reaction mixture that comprises a fucose donor moiety and the second fucosyltransferase under appropriate conditions to transfer fucose from the fucose donor moiety to the second acceptor moiety, such that the glycopeptide has a substantially uniform fucosylation pattern.

57. (New) A method for modifying the glycosylation pattern of a glycopeptide comprising a first acceptor moiety for a first fucosyltransferase and a second acceptor moiety for a second fucosyltransferase, wherein the glycopeptide is contacted with the first fucosyltranferase and the second fucosyltransferase simultaneously, said method comprising:

(a) contacting the glycopeptide with a reaction mixture that comprises a fucose donor moiety and the first fucosyltransferase under appropriate conditions to transfer fucose from the fucose donor moiety to the first acceptor moiety, such that the glycopeptide has a substantially uniform fucosylation pattern, and

(b) contacting the glycopeptide with a reaction mixture that comprises a fucose donor moiety and the second fucosyltransferase under appropriate conditions to transfer fucose from the fucose donor moiety to the second acceptor moiety, such that the glycopeptide has a substantially uniform fucosylation pattern.

58. (New) A method for modifying the glycosylation pattern of a glycopeptide comprising a first acceptor moiety for a first fucosyltransferase and a second acceptor moiety for a second fucosyltransferase, wherein the glycopeptide is contacted with the first fucosyltransferase and the second fucosyltransferase sequentially without isolation of product resulting from contacting with the first fucosyltransferase, said method comprising:

(a) contacting the glycopeptide with a reaction mixture that comprises a fucose donor moiety and the first fucosyltransferase under appropriate conditions to transfer fucose from the fucose donor moiety to the first acceptor moiety, such that the glycopeptide has a substantially uniform fucosylation pattern, and

(b) contacting the glycopeptide with a reaction mixture that comprises a fucose donor moiety and the second fucosyltransferase under appropriate conditions to transfer fucose from the fucose donor moiety to the second acceptor moiety, such that the glycopeptide has a substantially uniform fucosylation pattern.

59. (New) A method for modifying the glycosylation pattern of a glycopeptide comprising an acceptor moiety for a first fucosyltransferase, wherein the first fucosyltransferase is a member selected from FucT-IV, FucT-VI, FucT-VII and combinations thereof, said method comprising:

contacting the glycopeptide with a reaction mixture that comprises a fucose donor moiety and the first fucosyltransferase under appropriate conditions to transfer fucose from the fucose donor moiety to the acceptor moiety, such that the glycopeptide has a substantially uniform fucosylation pattern.

60. (New) A method for modifying the glycosylation pattern of a glycopeptide comprising a first acceptor moiety for a first fucosyltransferase and a second acceptor moiety for a second fucosyltransferase, wherein the second fucosyltransferase is a member selected from FucT-IV, FucT-VI, FucT-VII and combinations thereof, said method comprising:

(a) contacting the glycopeptide with a reaction mixture that comprises a fucose donor moiety and the first fucosyltransferase under appropriate conditions to transfer fucose from the fucose donor moiety to the first acceptor moiety, such that the glycopeptide has a substantially uniform fucosylation pattern, and

(b) contacting the glycopeptide with a reaction mixture that comprises a fucose donor moiety and the second fucosyltransferase under appropriate conditions to transfer fucose from the fucose donor moiety to the second acceptor moiety, such that the glycopeptide has a substantially uniform fucosylation pattern.

61. (New) A method for modifying the glycosylation pattern of a glycopeptide comprising an acceptor moiety for a first fucosyltransferase, wherein the first fucosyltransferase is recombinantly produced, said method comprising:

contacting the glycopeptide with a reaction mixture that comprises a fucose donor moiety and the first fucosyltransferase under appropriate conditions to transfer fucose from the fucose donor moiety to the acceptor moiety, such that the glycopeptide has a substantially uniform fucosylation pattern.

62. (New) The method according to claim **61**, wherein said first fucosyltransferase lacks a membrane anchoring domain.

63. (New) A method for modifying the glycosylation pattern of a glycopeptide comprising an acceptor moiety for a first fucosyltransferase wherein the glycopeptide is an IgG chimera, said method comprising:

contacting the glycopeptide with a reaction mixture that comprises a fucose donor moiety and the first fucosyltransferase under appropriate conditions to transfer fucose from the fucose donor moiety to the acceptor moiety, such that the glycopeptide has a substantially uniform fucosylation pattern.

64. (New) A method for modifying the glycosylation pattern of a glycopeptide comprising an acceptor moiety for a first fucosyltransferase, said method comprising:

(a) contacting said glycoprotein with a glycosyltransferase other than a fucosyltransferase and a donor moiety other than a fucose donor moiety, thereby glycosylating the glycoprotein with a glycosyl moiety other than a fucose unit, and

(b) contacting the glycopeptide with a reaction mixture that comprises a fucose donor moiety and the first fucosyltransferase under appropriate conditions to transfer fucose from the fucose donor moiety to the acceptor moiety, such that the glycopeptide has a substantially uniform fucosylation pattern.

65. (New) A method for modifying the glycosylation pattern of a glycopeptide comprising an acceptor moiety for a first fucosyltransferase, said method comprising:

(a) contacting said glycoprotein with a glycosyltransferase other than a fucosyltransferase and a donor moiety other than a fucose donor moiety, thereby glycosylating the glycoprotein with a glycosyl moiety other than a fucose unit, wherein the glycosyltransferase is a member selected from the group consisting of galactosyltransferase, sialyltransferase and combinations thereof, and

(b) contacting the glycopeptide with a reaction mixture that comprises a fucose donor moiety and the first fucosyltransferase under appropriate conditions to transfer

fucose from the fucose donor moiety to the acceptor moiety, such that the glycopeptide has a substantially uniform fucosylation pattern.